

UCSF/UCB Center for Engineering Cellular Control Systems

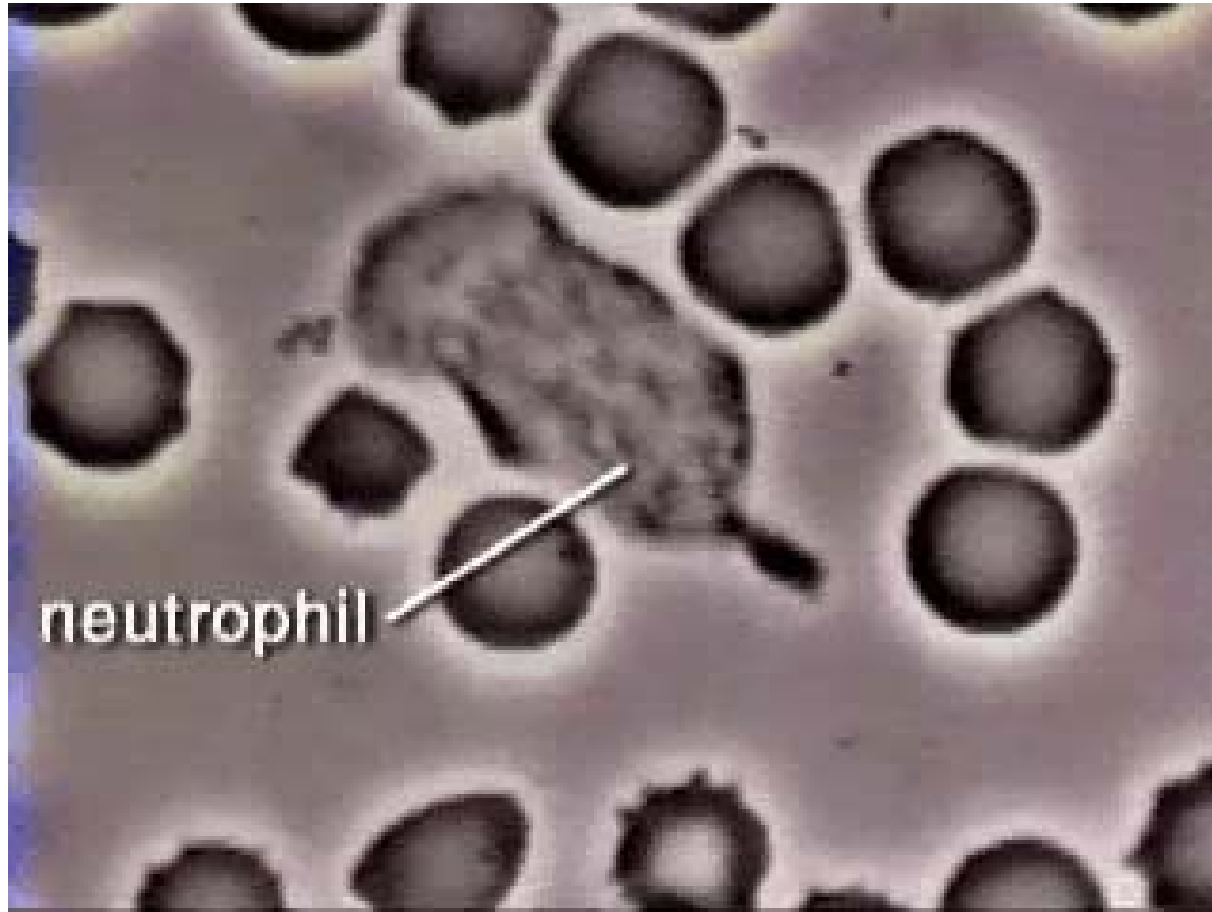


An NIH Nanomedicine Development Center

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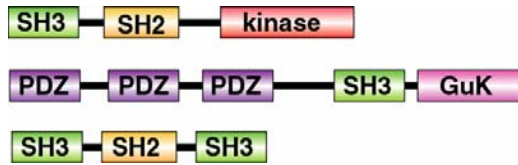
Nanomedicine challenges



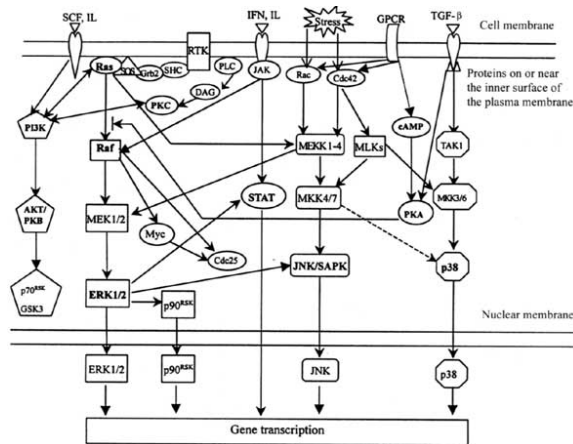
D. Rogers

**Can cellular control systems be engineered
for therapeutic applications?**

Cellular systems are modular



PARTS



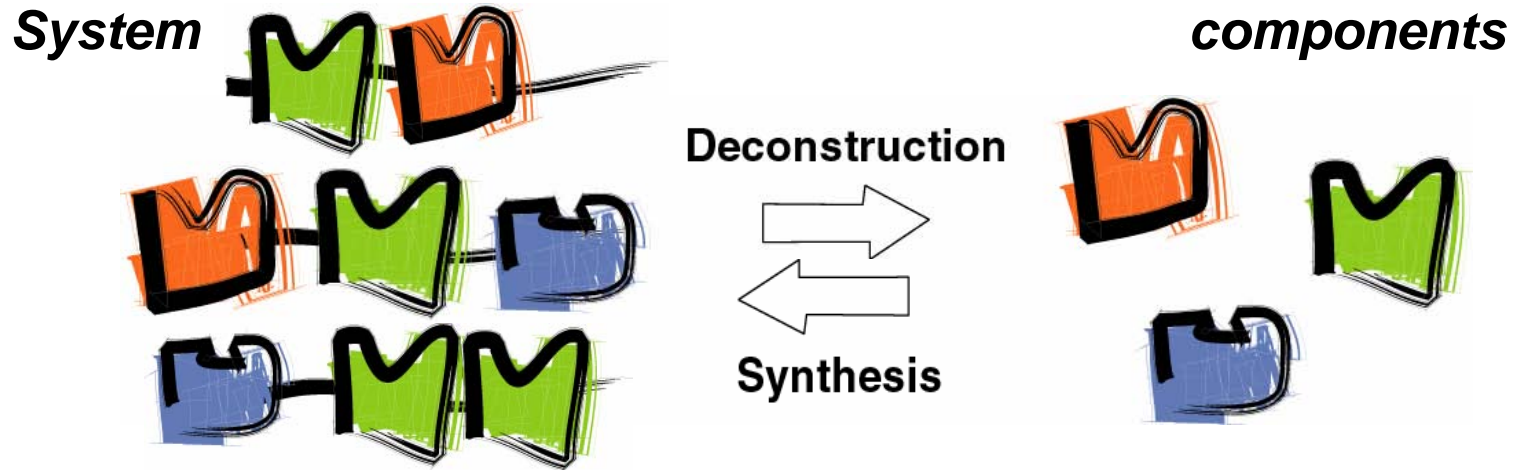
DEVICES



SYSTEMS



Why engineer cells?



UNDERSTANDING

Elucidate core design principles underlying complex biological function

- Minimal/alternative designs
- tools for precise manipulation of biological systems

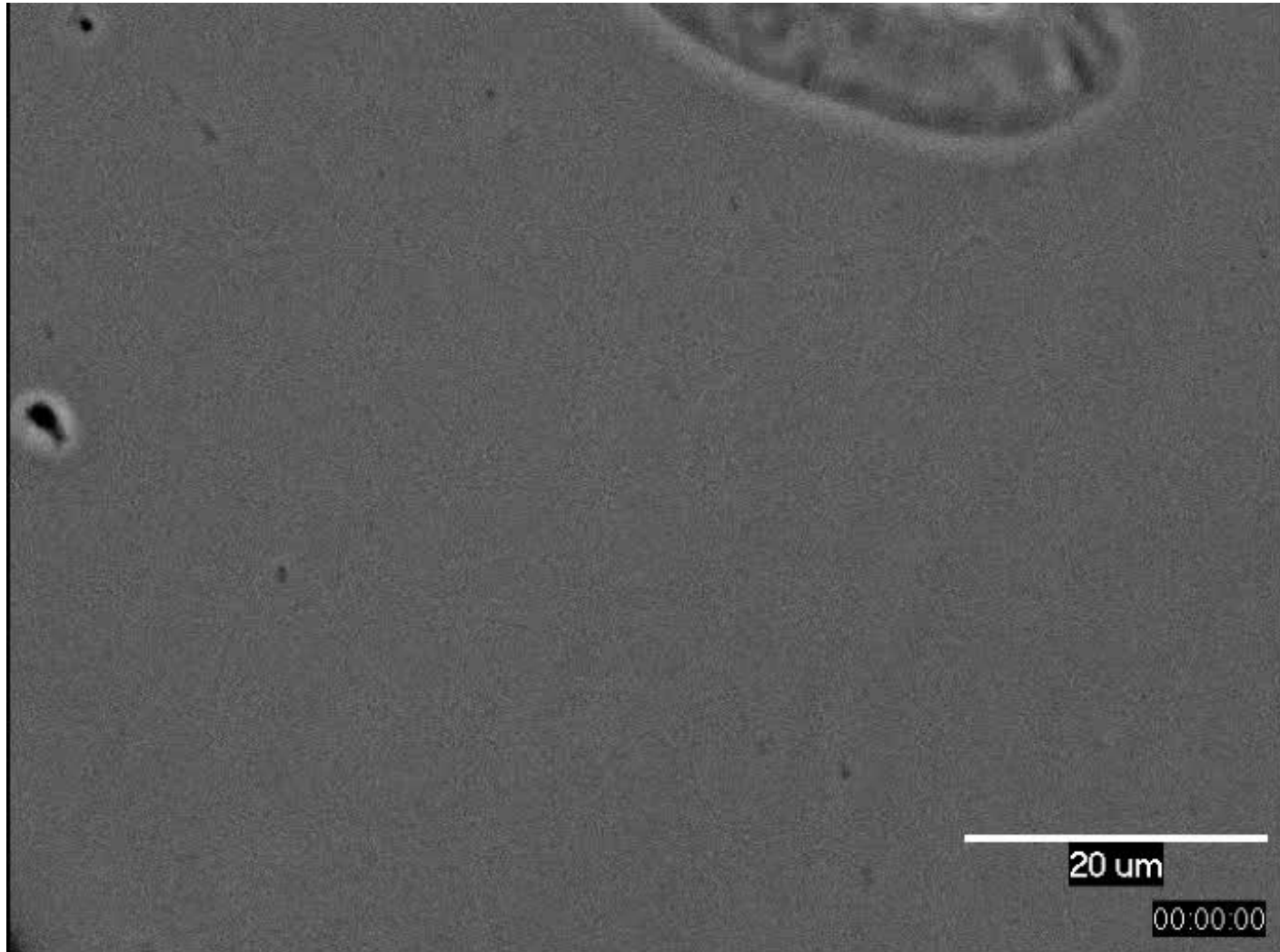
(physics, chemistry, etc.: understanding & manipulating system are coupled)

APPLICATIONS

Can we build cells with novel, therapeutic functions?

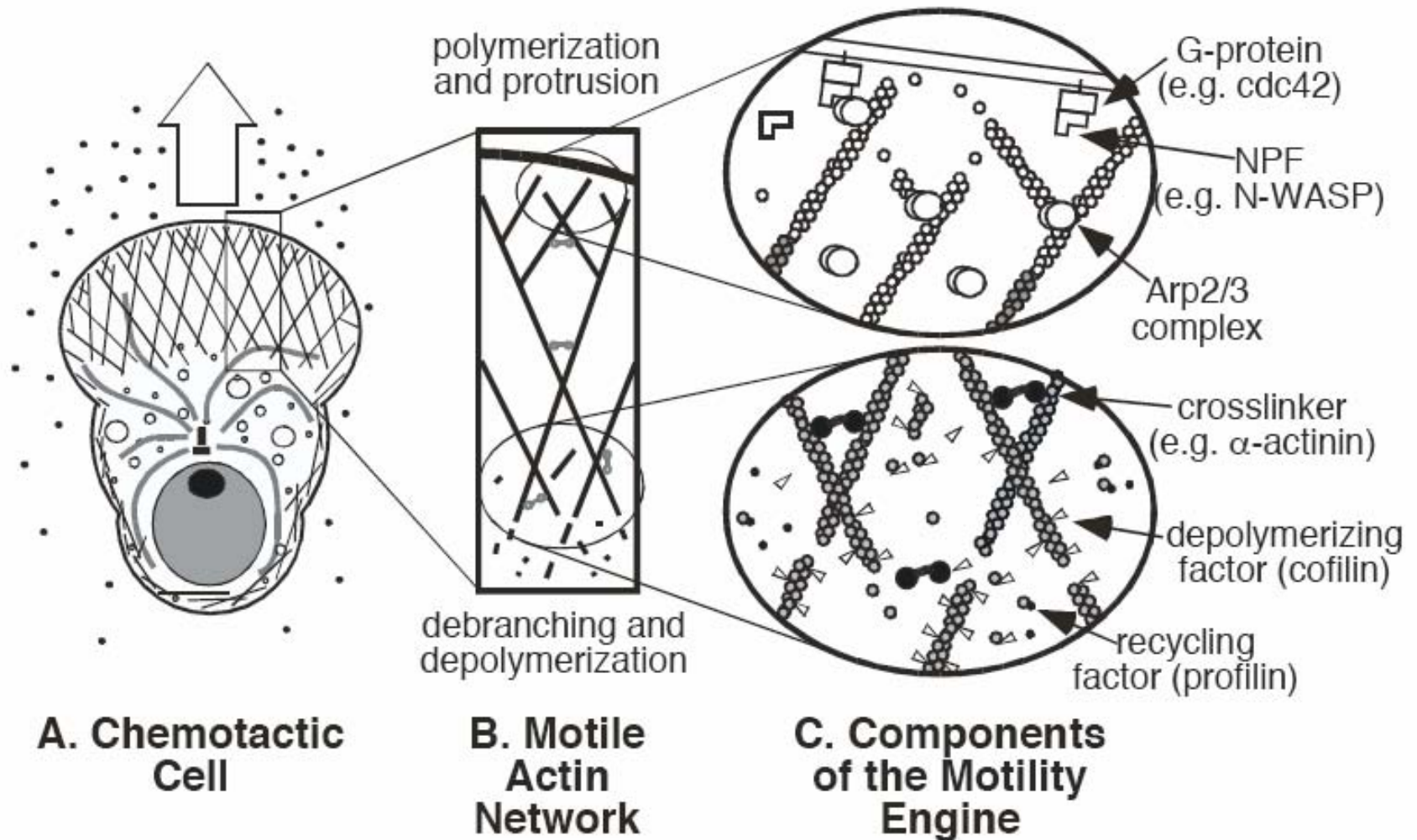
New generation of therapeutics: cellular machines/devices.

Test bed: Actin-based motility

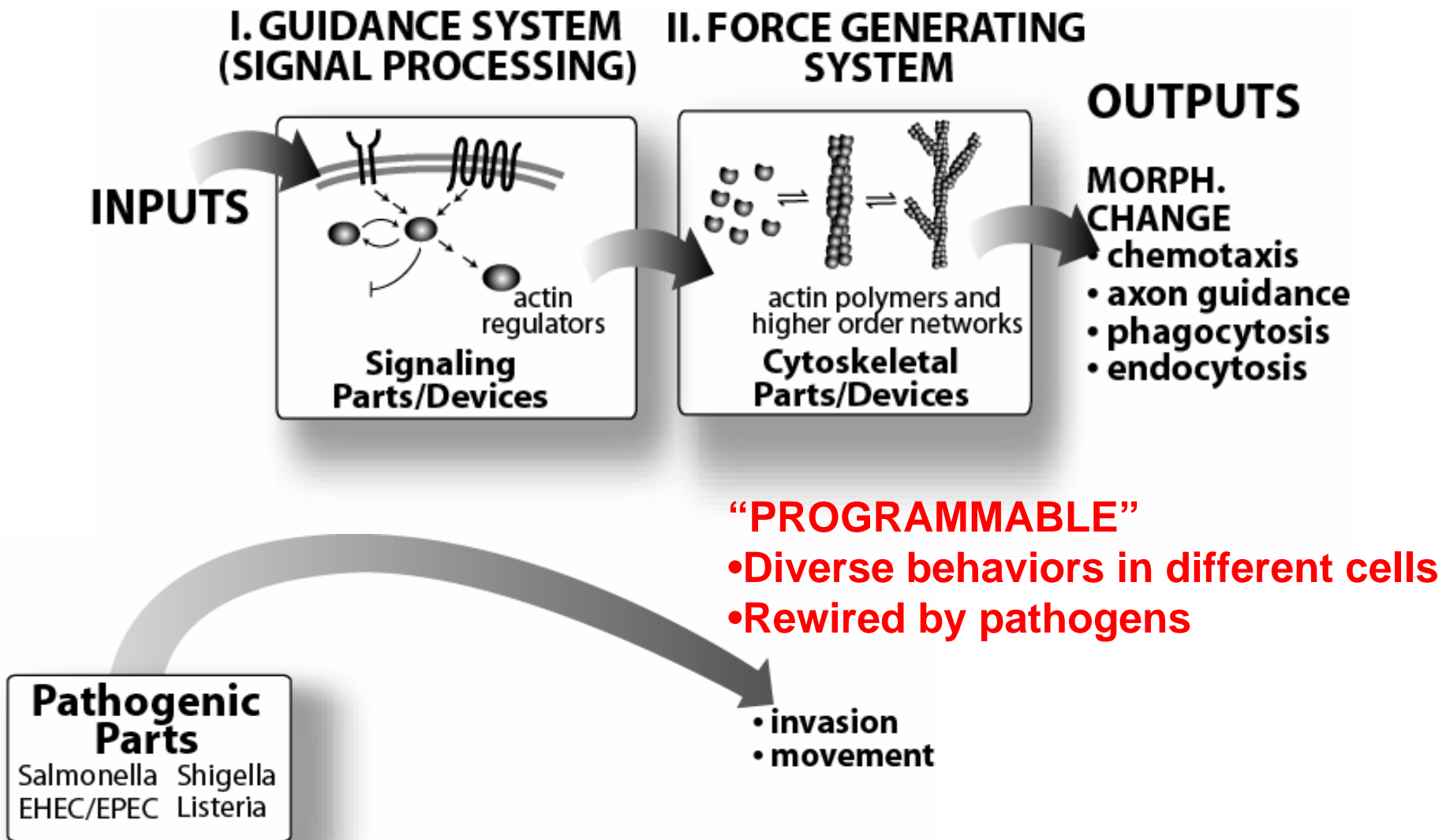


A. Liu

Complexity challenge: More is different



Test bed: Actin-based motility



Can we program cell movements?

- **What are design principles of guidance, polarization systems?**

spatio-temporal signal processing

- **What are design principles of cellular force generation systems?**

regulated polymerization, assembly

LONG-TERM APPLICATIONS:

- **Redirect cell targeting (axons, wound healing, immune cells)**
- **Search & delivery particles**

“The Cell Propulsion Lab”

GRAND CHALLENGES

1. Reprogram cellular guidance systems

Wendell Lim

2. Build alternative force generation systems

Dyche Mullins

3. Build synthetic assemblies capable of regulated shape change or motility

Dan Fletcher

TECHNICAL PILLARS

**Toolkit
(Mol. Parts)**

Tanja Kortemme

Assays

Orion Weiner

Modeling

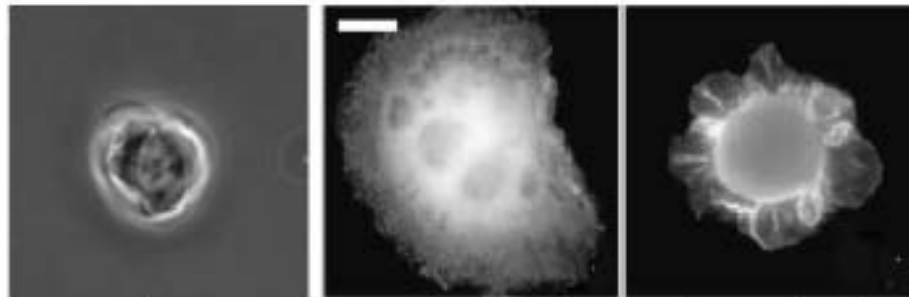
Chris Voigt

webpage

UCSF/UCB Nanomedicine Fellows

Challenge 1 : Reprogramming Guidance Systems

Drosophila S2 cells: NON-MOTILE
BUT show Rac and Rho induce spreading or contraction



native

Rac activation

Rho activation

spherical

symmetric
spreading

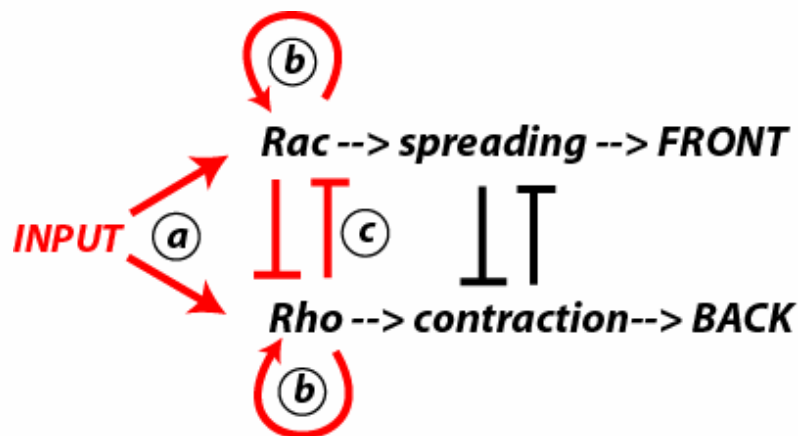
symmetric
contraction

HL-60 cells: MOTILE
Rac/Rho-dependent



*polarization of protrusion
vs contraction*

Rac - FRONT, spreading
Rho - BACK, contraction



**Can we make S2 cells
polarize?**

a. Input control

b. Local positive feedback

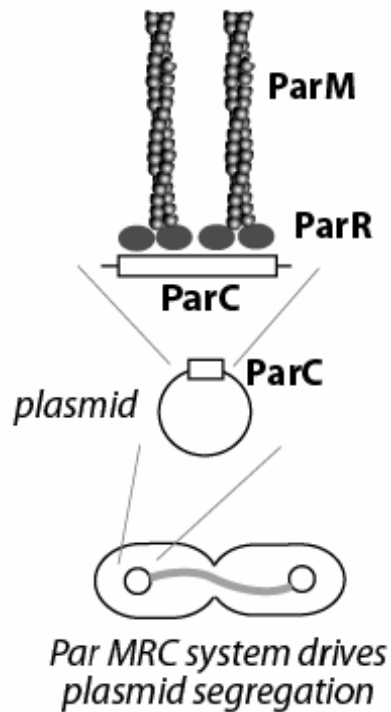
**c. Cross-inhibition of front/back
mediators**

Challenge 2 :

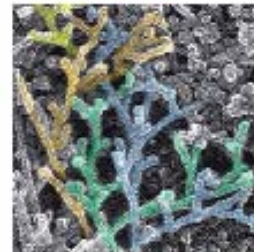
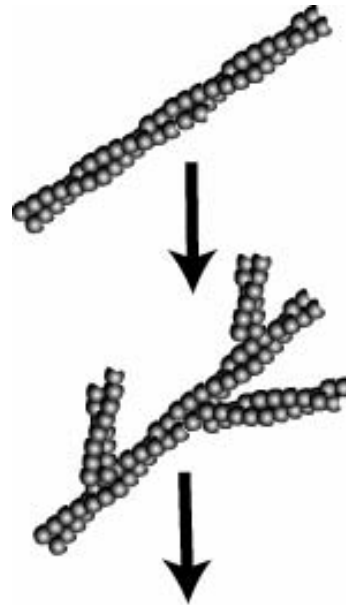
Build alternative force generation systems

BACTERIAL POLYMER:

ParM



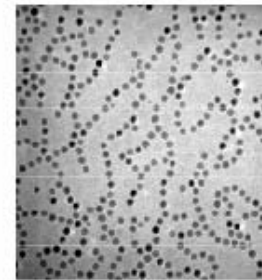
Mullins



actin network

Borisy

NANOPARTICLES:



magnetic particle polymers
(cobalt, iron oxide)



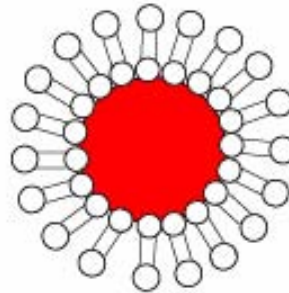
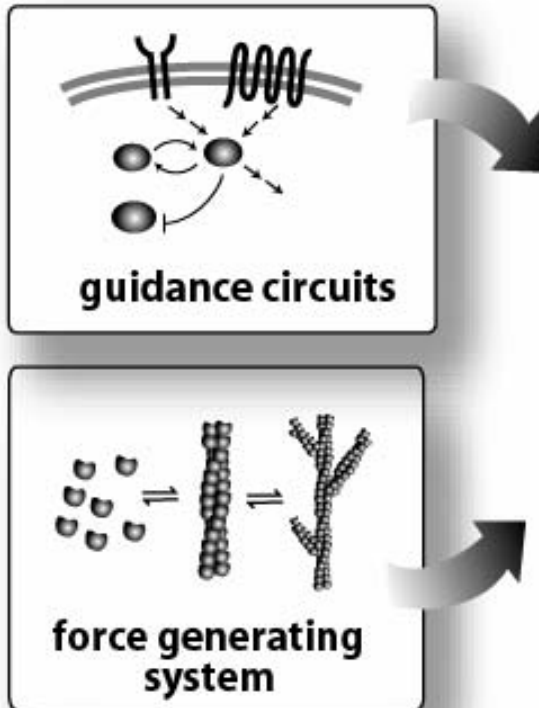
tetrapods
(cadmium selenide)

Alivisatos

What is required for a polymer system to move specific loads?

Challenge 3 :

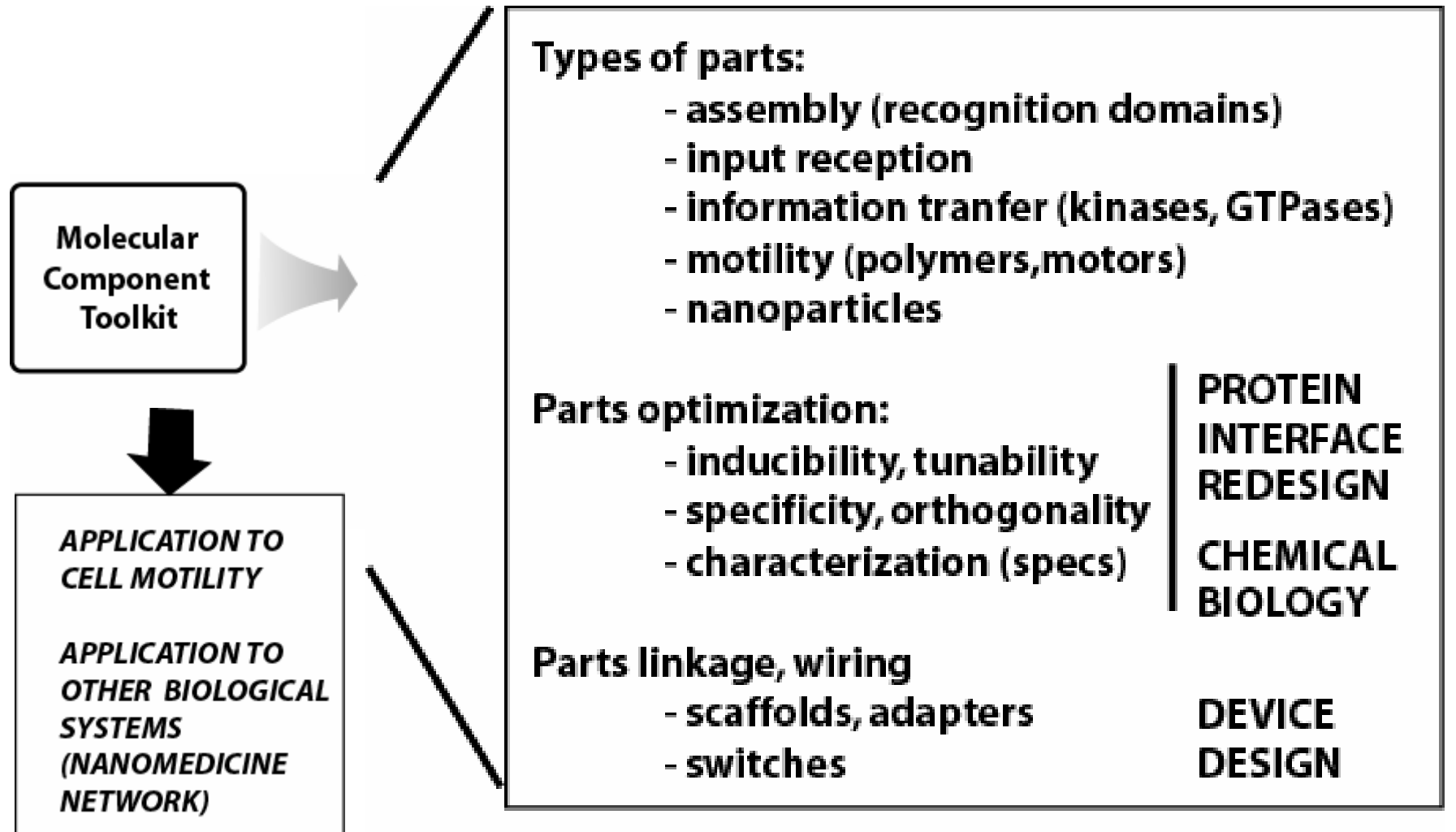
Build synthetic assemblies capable of regulated shape change or motility



assemble vesicles containing guidance and force systems to generate:

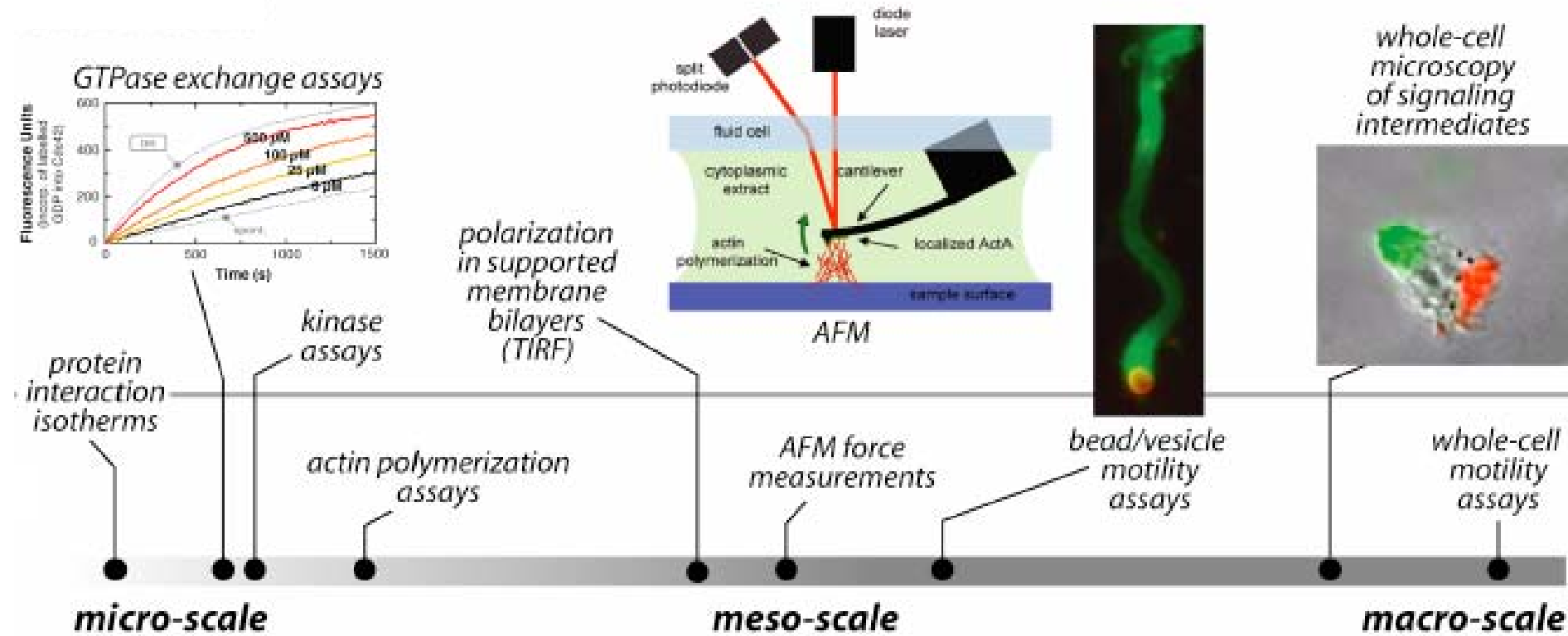
- 1) signal induced actin polymerization
(*ARTIFICIAL PLATELET*)
- 2) polarization/motility
- 3) directional motility
(*SEARCH & DELIVERY VEHICLE*)

Toolkit as a basis for design



Online registry of parts

Assays for micro to macro analysis



Apply, develop, & share technologies: Optical microscopy
Force microscopy
Fabrication & assembly

Modeling of control systems

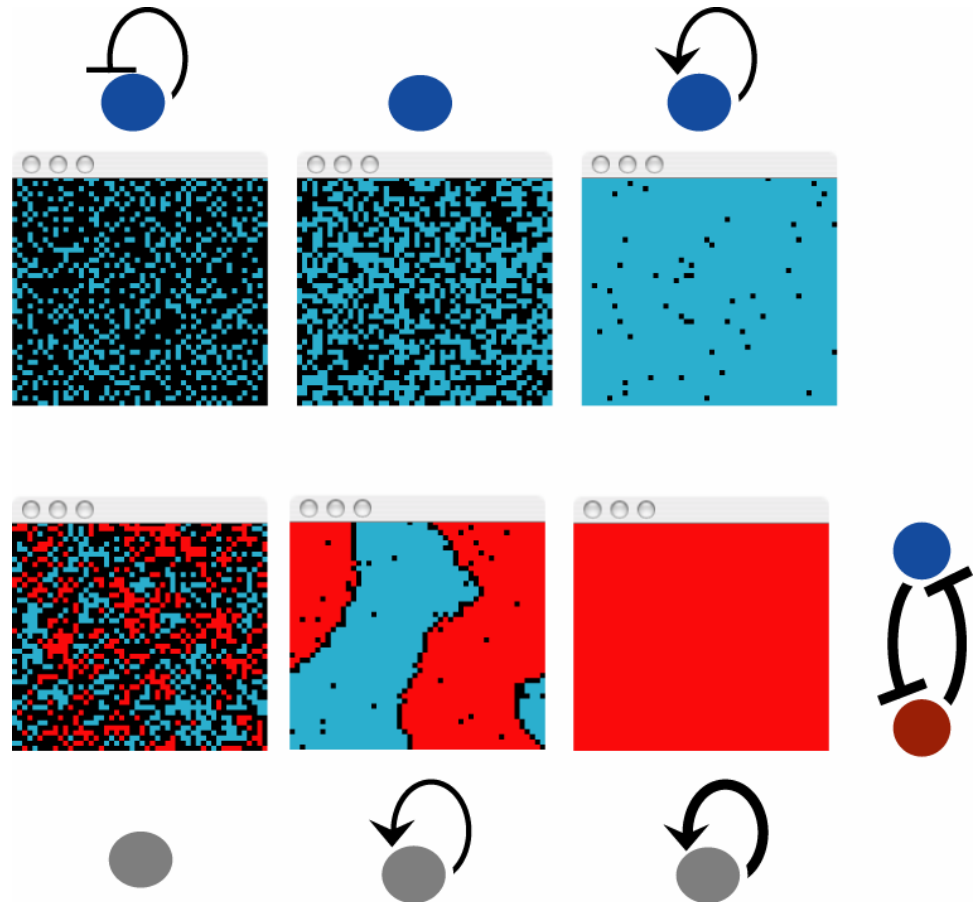
MODELING: Develop simple lattice-based platform for analyzing polarization circuits (Voigt, Arkin, Lim)

What circuits yield stable polarization?

Monte Carlo simulations with simplified energy function

Variables:

- *Feedback (sign/strength)*
- *cross inhibition*
- *Number of components*
- *Local vs. long-range*
- *Circuit connectivity*





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Challenge 1

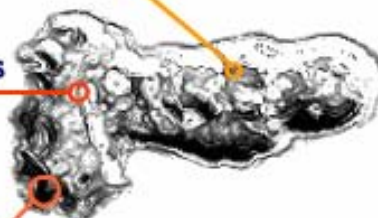
Reprogram cell guidance systems

Challenge 2

Build alternative force generating systems

Challenge 3

Engineer synthetic motility systems



Our goal is to understand the fundamental design principles of cellular control systems and to apply these principles to engineer cells or cell-like devices with novel "smart" therapeutic functions.

To achieve this goal, we are focusing on cell motility as a testbed system. Our multi-disciplinary team is focused on three engineering **grand challenges**, shown to the left.

[home](#) || [grand challenges](#) || [technical pillars](#) || [investigators](#) || [how to join](#) || [QB3](#) || [NIH Nanomedicine Development Program](#)

www.qb3.org/cpl